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MAGNITUDE OF BLOOD PRESSURE REDUCTION IN THE PLACEBO ARMS OF MODERN HYPERTENSION TRIALS: IMPLICATIONS FOR TRIALS OF RENAL DENERVATION

Poster Contributions
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Background: Early phase studies of novel interventions for hypertension, such as renal sympathetic denervation, are sometimes single-armed (uncontrolled). We explored the wisdom of this by quantifying the blood pressure fall in the placebo arms of contemporary trials of hypertension.

Methods: We searched Medline up to June 2014 and identified blinded, randomised trials of hypertension therapy in which the control arm received placebo medication or a sham (placebo) procedure. For non-resistant hypertension, we identified all such trials of drugs licensed by the US Food and Drug Administration (FDA) since 2000 (five drugs). This FDA-related restriction was not applied to resistant hypertension trials.

Results: This produced 7451 patients who were allocated to a blinded control from 52 trials of non-resistant hypertension, and 694 patients from 8 trials of resistant hypertension (three drugs and two interventions). Systolic blood pressure fell by 5.92mmHg (95% CI: 5.14-6.71; p<0.00001) in the non-resistant cohort and by 8.76 mmHg (95% CI: 4.83-12.70; p<0.0001) in the resistant cohort. Using meta-regression, the falls were larger in trials that did not use ambulatory blood pressure monitoring as an inclusion criterion (z=2.84, p=0.0045) and those where the patients were prescribed a continuous background of anti-hypertensives (z=-2.72, p=0.0065).

Conclusion: The non-trivial magnitude of these apparent blood pressure reductions with perfectly ineffective intervention (placebo) illustrates that efficacy explorations of novel therapies for hypertension, once safety is established, should be performed with a randomised, appropriately controlled and blinded design.